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=> d his ful

     FILE 'REGISTRY' ENTERED AT 18:22:04 ON 21 JAN 2005
                  E HH-AG 1.1/CN
L1             3 SEA ABB=ON  ("HH-AG 1.1"/CN OR "HH-AG 1.2"/CN OR "HH-AG
                  1.3"/CN) See attached displays

     FILE 'HCAPLUS' ENTERED AT 18:22:44 ON 21 JAN 2005
L2             8 SEA ABB=ON  L1 OR HH(W)AG(W)1
L3             8 SEA ABB=ON  L1 OR HH(W)AG(W)(1.1 OR 1.2 OR 1.3)
L4             1 SEA ABB=ON  L3 AND (?BRAIN?(W)(?PROGENITOR?(W)?CELL?(W)?DIVISIO
                  N? OR ?CELL?(W)?BIRTH?) OR ?NEUROGENES? OR ?BRDU?)

     FILE 'REGISTRY' ENTERED AT 18:26:11 ON 21 JAN 2005
                  E BROMODEOXYURIDINE/CN
L5             1 SEA ABB=ON  BROMODEOXYURIDINE/CN

     FILE 'HCAPLUS' ENTERED AT 18:26:26 ON 21 JAN 2005
L6             0 SEA ABB=ON  L3 AND (L5 OR ?BROMODEOXYURIDINE? OR ?BRDU?)(L)(?BR
                  AIN? OR ?NEURAL? OR ?NEURO?)
L7             0 SEA ABB=ON  L3 AND (L5 OR ?BROMODEOXYURIDINE? OR ?BRDU?)
L8             8 SEA ABB=ON  L3 OR L4
L9             0 SEA ABB=ON  L8 AND NON?(W)?HUMAN?
L10            2 SEA ABB=ON  L8 AND (?INCREAS? OR ?STIMUL? OR ?IMPROV? OR
                  ?ENHANC?)
L11            8 SEA ABB=ON  L8 OR L10  8 cits from CA Plus

     FILE 'MEDLINE, BIOSIS, EMBASE, JAPIO, JICST-EPLUS' ENTERED AT 18:29:58 ON
     21 JAN 2005
L12            0 SEA ABB=ON  L11  0 cits from other db's
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Registry search for Hh-Ag 1.3


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YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:y


L1   ANSWER 1 OF 3  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   364590-63-6  REGISTRY
CN   Benzo[b]thiophene-2-carboxamide, 3-chloro-N-[4-(methylamino)cyclohexyl]-N-
     [[3-(4-pyridinyl)phenyl]methyl]- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Hh-Ag 1.3
FS   3D CONCORD
MF   C28 H28 Cl N3 O S
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA  CAplus document type:  Journal; Patent
RL.P   Roles from patents:  BIOL (Biological study); PREP (Preparation); USES
       (Uses)
RLD.P  Roles for non-specific derivatives from patents:  BIOL (Biological
       study); USES (Uses)
RL.NP  Roles from non-patents:  BIOL (Biological study); USES (Uses)
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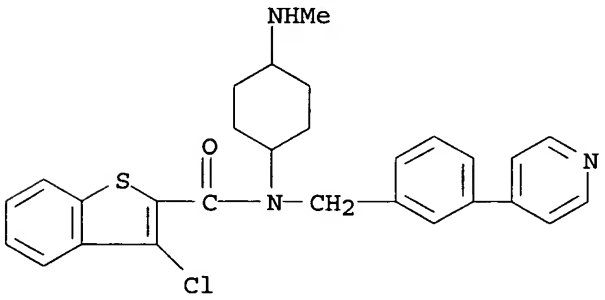


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

               6 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
               6 REFERENCES IN FILE CAPLUS (1907 TO DATE)
ED   Entered STN:  25 Oct 2001

L1   ANSWER 2 OF 3  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   364590-54-5  REGISTRY
CN   Benzo[b]thiophene-2-carboxamide, 3-chloro-N-[(4'-cyano-6-methoxy[1,1'-
     biphenyl]-3-yl)methyl]-N-[4-(methylamino)cyclohexyl]- (9CI)  (CA INDEX
     NAME)
OTHER NAMES:
CN   Hh-Ag 1.2
FS   3D CONCORD
MF   C31 H30 Cl N3 O2 S
CI   COM
SR   CA
LC   STN Files:   CA, CAPLUS, PROUSDDR, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
DT.CA  CAplus document type:  Journal; Patent
RL.P   Roles from patents:  BIOL (Biological study); PREP (Preparation); USES
       (Uses)
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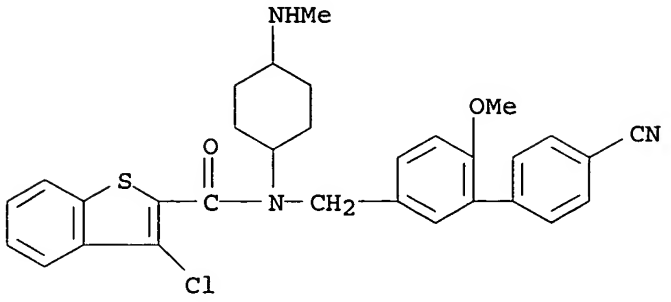
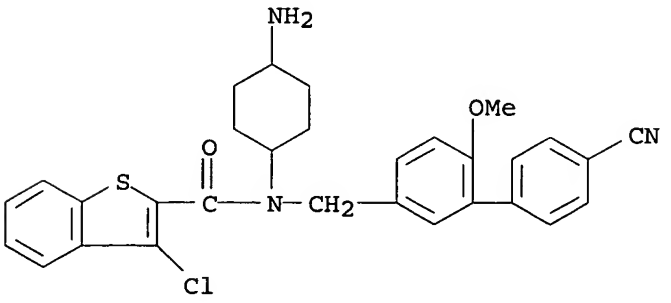
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7 REFERENCES IN FILE CAPLUS (1907 TO DATE)
ED Entered STN: 25 Oct 2001

L1 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN
RN 364590-52-3 REGISTRY
CN Benzo[b]thiophene-2-carboxamide, N-(4-aminocyclohexyl)-3-chloro-N-[(4'-cyano-6-methoxy[1,1'-biphenyl]-3-yl)methyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Hh-Ag 1.1**
FS 3D CONCORD
MF C30 H28 Cl N3 O2 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)
ED Entered STN: 25 Oct 2001

=> d ibib abs l11 1-8

L11 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:634046 HCAPLUS
DOCUMENT NUMBER: 141:167820
TITLE: **Brain progenitor cell division**-modulating agent assay, and related therapeutic methods and compositions
INVENTOR(S): Hen, Rene; Santarelli, Luca; Saxe, Michael
PATENT ASSIGNEE(S): The Trustees of Columbia University In the City of New York, USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004065567	A2	20040805	WO 2004-US1751		20040122
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI					
US 2004247525	A1	20041209	US 2004-764068		20040122
PRIORITY APPLN. INFO.:			US 2003-442081P	P	20030123
			US 2003-526190P	P	20031201

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides methods for determining whether an agent **increases brain progenitor cell division** in a subject. The invention also provides methods for treating anxiety, depression, a cognitive disorder or a neurodegenerative disorder or inhibiting the onset of anxiety, depression or a cognitive disorder by administering to an afflicted subject a therapeutically or prophylactically effective amount of the agent. The invention further provides methods for treating anxiety, depression, cognitive disorder or a neurodegenerative disorder or inhibiting the onset of anxiety, depression or a cognitive disorder by administering to an afflicted subject a therapeutically or prophylactically effective amount of **Hh-Ag 1.1** (I), **Hh-Ag 1.2** (II), **Hh-Ag 1.3** (III), or derivs. thereof.

L11 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:473330 HCAPLUS
DOCUMENT NUMBER: 141:33772
TITLE: Hedgehog antagonists, methods and therapeutic use
INVENTOR(S): Dudek, Henryk; Karavanov, Irina; Pepicelli, Carmen; Kotkow, Karen; Rubin, Lee L.
PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 150 pp., Cont.-in-part of U.S. Pat. Appl. 2004 60,568.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004110663	A1	20040610	US 2003-652298		20030829
US 2002165221	A1	20021107	US 2001-977096		20011012
PRIORITY APPLN. INFO.:			US 2000-240564P	P	20001013
			US 2001-977864	A2	20011015
			US 2002-407145P	P	20020829
			US 2000-240536P	P	20001013

AB The invention discloses compns. and methods for inhibiting angiogenesis and treating or preventing unwanted cell proliferation, including tumors, by inhibiting the hedgehog pathway, e.g., with an antagonist of the hedgehog pathway. Hedgehog antagonists include small mols., antibodies, antisense nucleic acids, etc.

L11 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:203948 HCAPLUS
DOCUMENT NUMBER: 140:247034
TITLE: Hedgehog antagonists for inhibiting angiogenesis and treating or preventing unwanted cell proliferation, including tumors
INVENTOR(S): Dudek, Henryk K.; Karavanov, Irina; Pepicelli, Carmen; Rubin, Lee; Kotkow, Karen
PATENT ASSIGNEE(S): Curis, Inc., USA
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004020599	A2	20040311	WO 2003-US27279	20030829
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2002-407145P	P 20020829

AB The invention discloses compns. and methods for inhibiting angiogenesis and treating or preventing unwanted cell proliferation, including tumors, by inhibiting the hedgehog pathway, e.g., with an antagonist of the hedgehog pathway. Antagonists include e.g. antibodies and antisense nucleic acids.

L11 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:570651 HCAPLUS

DOCUMENT NUMBER: 139:133461
TITLE: Preparation of substituted benzothiophenes as regulators of cell proliferation
INVENTOR(S): Baxter, Anthony David; Boyd, Edward Andrew; Frank-Kamenetsky, Maria; Guicherit, Oivin; Porter, Jeffery; Price, Stephen; Rubin, Lee; Stibbard, John Harry Alexander
PATENT ASSIGNEE(S): Curis, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 137 pp., Cont.-in-part of U.S. Ser. No. 964,276.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003139457	A1	20030724	US 2002-245844	20020917
US 6683108	B1	20040127	US 2000-724492	20001128
WO 2001074344	A2	20011011	WO 2001-US10296	20010330
WO 2001074344	A3	20020523		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002198236	A1	20021226	US 2001-964276	20010926
US 6683192	B2	20040127		

PRIORITY APPLN. INFO.:

US 2000-193279P	P	20000330
US 2000-724492	A2	20001128
WO 2001-US10296	A2	20010330
US 2001-964276	A2	20010926
US 2000-724955	A	20001128

OTHER SOURCE(S): MARPAT 139:133461
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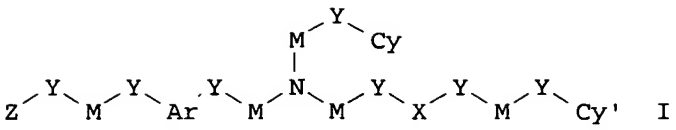

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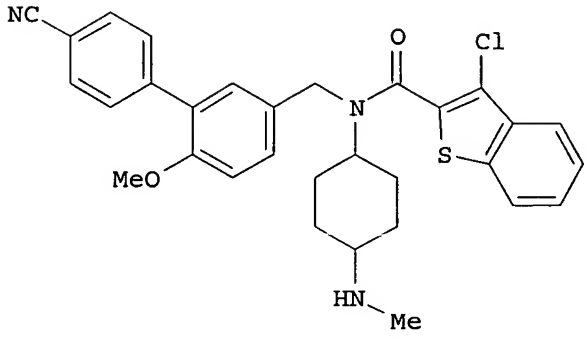


II

AB Title compds. I [Ar = (un)substituted (hetero)aryl; X = CO, CS, SO2, SO, etc.; Y = absent for each occurrence; Z = absent, (un)substituted aryl, carbocycle, hetercycle, heteroaryl, etc.; M = independently for each occurrence (un)substituted methylene, etc.; Cy = (un)substituted (hetero)aryl, heterocycle, cycloalkyl, polycyclic group; Cy' = 3-chlorobenzo[b]thiophen-2-yl, etc.] are prepared For instance, (4-aminocyclohexyl)carbamic acid tert-Bu ester (preparation given) is condensed with 3-(4-cyanophenyl)-4-methoxybenzaldehyde ((MeO)3CH, NaBH(OAc)3) and the resulting amine acylated with 3-chlorobenzo[b]thiophene-2-carbonyl chloride and finally deprotected to give II as the HCl salt. Example compds. were shown to be hedgehog agonists. I are used to modulate proliferation or differentiation in a cell or tissue.

L11 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:93513 HCAPLUS
DOCUMENT NUMBER: 139:301950
TITLE: Small-molecule modulators of Hedgehog signaling: identification and characterization of Smoothened agonists and antagonists
AUTHOR(S): Frank-Kamenetsky, Maria; Zhang, Xiaoyan M.; Bottega, Steve; Guicherit, Oivin; Wichterle, Hynek; Dudek, Henryk; Bumcrot, David; Wang, Frank Y.; Jones, Simon; Shulok, Janine; Rubin, Lee L.; Porter, Jeffery A.
CORPORATE SOURCE: Curis, Inc., Cambridge, MA, 02138, USA
SOURCE: Journal of Biology (London, United Kingdom) (2002), 1(2), No pp. given
CODEN: JBOIAW; ISSN: 1475-4924
URL: http://jbiol.com/content/1/2/10
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The Hedgehog (Hh) signaling pathway is vital to animal development as it mediates the differentiation of multiple cell types during embryogenesis. In adults, Hh signaling can be activated to facilitate tissue maintenance

and repair. Moreover, **stimulation** of the Hh pathway has shown therapeutic efficacy in models of neuropathy. The underlying mechanisms of Hh signal transduction remain obscure, however: little is known about the communication between the pathway suppressor Patched (Ptc), a multipass transmembrane protein that directly binds Hh, and the pathway activator Smoothened (Smo), a protein that is related to G-protein-coupled receptors and is capable of constitutive activation in the absence of Ptc. We have identified and characterized a synthetic non-peptidyl small mol., Hh-Ag, that acts as an agonist of the Hh pathway. This Hh agonist promotes cell-type-specific proliferation and concentration-dependent differentiation in vitro, while in utero it rescues aspects of the Hh-signaling defect in Sonic hedgehog-null, but not Smo-null, mouse embryos. Biochem. studies with Hh-Ag, the Hh-signaling antagonist cyclopamine, and a novel Hh-signaling inhibitor Cur61414, reveal that the action of all these compds. is independent of Hh-protein ligand and of the Hh receptor Ptc, as each binds directly to Smo. Thus, Smo can have its activity modulated directly by synthetic small mols. These studies raise the possibility that Hh signaling may be regulated by endogenous small mols. in vivo and provide potent compds. with which to test the therapeutic value of activating the Hh-signaling pathway in the treatment of traumatic and chronic degenerative conditions.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:978471 HCAPLUS
DOCUMENT NUMBER: 138:39182
TITLE: Preparation of substituted benzothiophene derivatives as hedgehog agonists and regulators of cell proliferation and differentiation
INVENTOR(S): Baxter, Anthony David; Boyd, Edward Andrew; Guicherit, Oivin M.; Porter, Jeffery; Price, Stephen; Rubin, Lee; Stibbard, John Harry Alexander
PATENT ASSIGNEE(S): Curis, Inc., UK
SOURCE: U.S. Pat. Appl. Publ., 130 pp., Cont.-in-part of U.S. Ser. No. 724,492.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002198236	A1	20021226	US 2001-964276	20010926
US 6683192	B2	20040127		
US 6683108	B1	20040127	US 2000-724492	20001128
US 2003139457	A1	20030724	US 2002-245844	20020917
WO 2003027234	A2	20030403	WO 2002-US29522	20020918
WO 2003027234	A3	20031218		
WO 2003027234	C2	20040219		

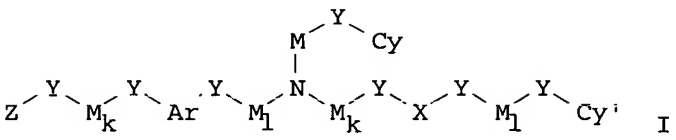
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,

CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1436287	A2	20040714	EP 2002-773438		20020918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
US 2005014796	A1	20050120	US 2003-732669		20031209
PRIORITY APPLN. INFO.:			US 2000-193279P	P	20000330
			US 2000-724492	A2	20001128
			WO 2001-US10296	A2	20010330
			US 2001-964276	A2	20010926
			WO 2002-US29522	W	20020918

OTHER SOURCE(S): MARPAT 138:39182

GI



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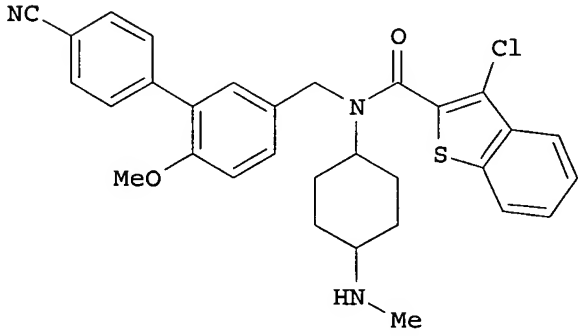

I

AB Title compds. I [Ar = (hetero)aryl; X = CO, CS, SO2, SO, CH2; Y = absent; Z = absent, aryl, carbocyclyl, heterocyclyl, etc.; M = (un)substituted methylene, etc.; Cy = aryl, heterocyclyl, heteroaryl, cycloalkyl; Cy' = 3-chlorobenzo[b]thiophen-2-yl, 3-fluorobenzo[b]thiophen-2-yl, etc.] are prepared For instance, N-(4-aminocyclohexyl)-N-methylcarbamic acid tert-Bu ester (preparation given) was alkylated with 5'-formyl-2'-methoxy-[1,1'-Biphenyl]-4-carbonitrile (MeO3CH, NaBH(OAc)3) and the resulting adduct acylated with 3-chlorobenzo[b]thiophene-2-carbonyl chloride and finally deprotected to give II, which was isolated as the hydrochloride. Methods and reagents are provided for modulating proliferation or differentiation in a cell or tissue, comprising contacting the cell with a hedgehog agonist. I are used to correct or inhibit an aberrant or unwanted growth state, e.g., by antagonizing a normal ptc pathway or agonizing smoothened or hedgehog activity.

L11 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:859144 HCAPLUS
DOCUMENT NUMBER: 138:396125

TITLE: Small molecule modulation of Smoothened activity
AUTHOR(S): Chen, James K.; Taipale, Jussi; Young, Keith E.; Maiti, Tapan; Beachy, Philip A.
CORPORATE SOURCE: Department of Molecular Biology and Genetics, Howard Hughes Medical Institute, Johns Hopkins University School of Medicine, Baltimore, MD, 21205, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2002), 99(22), 14071-14076
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Smoothened (Smo), a distant relative of G protein-coupled receptors, mediates Hedgehog (Hh) signaling during embryonic development and can initiate or transmit ligand-independent pathway activation in tumorigenesis. Although the cellular mechanisms that regulate Smo function remain unclear, the direct inhibition of Smo by cyclopamine, a plant-derived steroidal alkaloid, suggests that endogenous small mols. may be involved. Here we demonstrate that SAG, a chlorobenzothiophene-containing Hh pathway agonist, binds to the Smo heptahelical bundle in a manner that antagonizes cyclopamine action. In addition, we have identified four small mols. that directly inhibit Smo activity but are structurally distinct from cyclopamine. Functional and biochem. studies of these compds. provide evidence for the small mol. modulation of Smo through multiple mechanisms and yield insights into the physiol. regulation of Smo activity. The mechanistic differences between the Smo antagonists may be useful in the therapeutic manipulation of Hh signaling.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:747593 HCAPLUS
DOCUMENT NUMBER: 135:283224
TITLE: Small organic molecule hedgehog agonists as regulators of cell proliferation and differentiation
INVENTOR(S): Baxter, Anthony David; Boyd, Edward Andrew; Guicherit, Oivin M.; Porter, Jeffrey; Price, Stephen; Rubin, Lee E.
PATENT ASSIGNEE(S): Curis, Inc., USA
SOURCE: PCT Int. Appl., 246 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074344	A2	20011011	WO 2001-US10296	20010330
WO 2001074344	A3	20020523		
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US 6613798	B1	20030902	US 2000-724955	20001128

US 6683108	B1	20040127	US 2000-724492	20001128
CA 2404413	AA	20011011	CA 2001-2404413	20010330
EP 1272168	A2	20030108	EP 2001-922914	20010330
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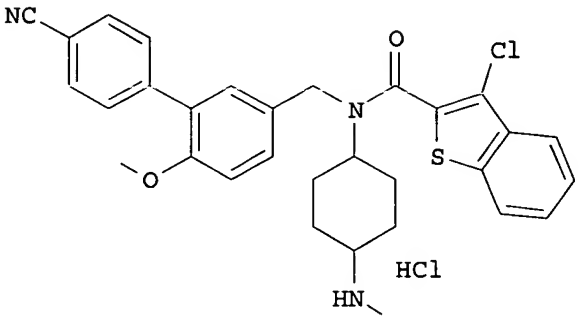
JP 2003535822	T2	20031202	JP 2001-572089	20010330
US 2003139457	A1	20030724	US 2002-245844	20020917
PRIORITY APPLN. INFO.:			US 2000-193279P	P 20000330
			US 2000-724492	A 20001128
			US 2000-724955	A 20001128
			WO 2001-US10296	W 20010330
			US 2001-964276	A2 20010926

OTHER SOURCE(S): MARPAT 135:283224

GI



I

AB Methods and reagents are provided for modulating proliferation or differentiation in a cell or tissue, comprising contacting the cell with a hedgehog agonist. In certain embodiments, the methods and reagents may be employed to correct or inhibit an aberrant or unwanted growth state, e.g., by antagonizing a normal ptc pathway or agonizing smoothened or hedgehog activity. Preparation of compds. (e.g. I) is described.